

Annex G3

Viability Summaries

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Table G3-1 Agonist Viability Summary for Phase 2a, 2b, and 3 Range Finder Experiments

Chemical	Phase	Laboratory	Minimum Cytotoxic Concentration (M) ^{a,b,c}	
			Exp 1	Exp 2
Diethylstilbestrol	2a	XDS	3.73×10^{-8}	
		ECVAM	3.73×10^{-4}	
		Hiyoshi	NR (3.73×10^{-5})	
Corticosterone	2a	XDS	2.89×10^{-3}	
		ECVAM	2.89×10^{-3}	
		Hiyoshi	2.89×10^{-3}	
Bisphenol A	2a	XDS	4.38×10^{-6}	
		ECVAM	4.38×10^{-5}	
		Hiyoshi	NR (4.38×10^{-4})	
Bisphenol B	2a	XDS	4.13×10^{-3}	
		ECVAM	4.13×10^{-3}	
		Hiyoshi	NR (4.13×10^{-3})	
Vinclozolin	2b	XDS	3.50×10^{-5}	
		ECVAM	NR (3.50×10^{-5})	
		Hiyoshi	NR (3.50×10^{-4})	
<i>p</i> -n-nonylphenol	2b	XDS	4.54×10^{-5}	
		ECVAM	(4.54×10^{-4})	
		Hiyoshi	NR (4.54×10^{-4})	
<i>o,p</i> '-DDT	2b	XDS	2.82×10^{-5}	
		ECVAM	2.82×10^{-4}	
		Hiyoshi	NR (2.82×10^{-5})	
Genistein	2b	XDS	3.70×10^{-4}	
		ECVAM	NR (3.70×10^{-4})	
		Hiyoshi	NR (3.70×10^{-4})	
Flavone	2b	XDS	NR (4.50×10^{-4})	
		ECVAM	4.50×10^{-4}	
		Hiyoshi	4.50×10^{-4}	

^aIf no cytotoxicity was reported, the highest concentration tested is reported in parenthesis

^bAfter the initial test was conducted, the laboratory changed the testing concentrations used, in order to more adequately cover the concentration-response curve

^cLaboratory voluntarily repeated testing.

Abbreviations: ECVAM = European Centre for the Validation of Alternative Methods;

Hiyoshi = Hiyoshi Corporation; M = molar; NR = Not Reported; XDS = Xenobiotic Detection Systems, Inc.

Table G3-1 Agonist Viability Summary for Phase 2a, 2b, and 3 Range Finder Experiments (Continued)

Chemical	Phase	Laboratory	Minimum Cytotoxic Concentration (M) ^{a,b,c}	
			Exp 1	Exp 2
Butyl benzyl phthalate	2b	XDS	3.20×10^{-4}	NR
		ECVAM	(3.20×10^{-5})	
		Hiyoshi	NR (3.20×10^{-5})	
Atrazine	2b	XDS	NR (4.64×10^{-4})	NR (4.64×10^{-4})
		ECVAM		NR (4.64×10^{-4})
		Hiyoshi		NR (4.64×10^{-4})
17α -ethynodiol	2b	XDS	3.37×10^{-4}	3.37×10^{-4}
		ECVAM		NR
		Hiyoshi		(3.37×10^{-5})
Tamoxifen	3	XDS	2.69×10^{-5}	2.69×10^{-5}
		ECVAM		2.69×10^{-5}
		Hiyoshi		2.69×10^{-5}
Resveratrol	3	XDS	4.38×10^{-4}	4.38×10^{-4}
		ECVAM		NR (4.38×10^{-4})
		Hiyoshi		
Raloxifene	3	XDS	1.96×10^{-4}	1.96×10^{-4}
		ECVAM		NR (1.96×10^{-5})
		Hiyoshi		
Propylthiouracil	3	XDS	5.87×10^{-3}	NR
		ECVAM		(5.87×10^{-3})
		Hiyoshi		NR (5.87×10^{-3})
Progesterone	3	XDS	3.18×10^{-4}	3.18×10^{-4}
		ECVAM		NR (3.18×10^{-5})
		Hiyoshi		
Phenolphthalin	3	XDS	3.12×10^{-3}	NR
		ECVAM		(3.12×10^{-3})
		Hiyoshi		3.12×10^{-3}

^aIf no cytotoxicity was reported, the highest concentration tested is reported in parenthesis

^bAfter the initial test was conducted, the laboratory changed the testing concentrations used, in order to more adequately cover the concentration-response curve

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Abbreviations: ECVAM = European Centre for the Validation of Alternative Methods; Hiyoshi = Hiyoshi Corporation; M = molar; NR = Not Reported; XDS = Xenobiotic Detection Systems, Inc.

Table G3-1 Agonist Viability Summary for Phase 2a, 2b, and 3 Range Finder Experiments (Continued)

Chemical	Phase	Laboratory	Minimum Cytotoxic Concentration (M) ^{a,b,c}	
			Exp 1	Exp 2
<i>p,p'</i> -DDE	3	XDS	3.14×10^{-5}	
		ECVAM	3.14×10^{-3}	
		Hiyoshi	NR (3.14×10^{-5})	
Methyl testosterone	3	XDS	2.89×10^{-3}	
		ECVAM	2.89×10^{-4}	2.89×10^{-4}
		Hiyoshi	NR (2.89×10^{-4})	
<i>meso</i> -hexestrol	3	XDS	3.70×10^{-4}	
		ECVAM	3.70×10^{-6}	3.70×10^{-4}
		Hiyoshi	NR (3.70×10^{-4})	
Kepone	3	XDS	2.04×10^{-4}	
		ECVAM	2.04×10^{-5}	2.04×10^{-4}
		Hiyoshi	NR (2.04×10^{-4})	
Kaempferol	3	XDS	3.49×10^{-4}	
		ECVAM	3.49×10^{-4}	3.49×10^{-3}
		Hiyoshi	NR (3.49×10^{-4})	
Hydroxyflutamide	3	XDS	3.42×10^{-4}	
		ECVAM	NR (3.42×10^{-4})	
		Hiyoshi	NR (3.42×10^{-4})	
Fluoranthene	3	XDS	4.94×10^{-4}	
		ECVAM	NR (4.94×10^{-4})	
		Hiyoshi	NR (4.94×10^{-5})	
Ethyl paraben	3	XDS	6.02×10^{-3}	
		ECVAM	6.02×10^{-3}	
		Hiyoshi	NR (6.02×10^{-4})	
Estrone	3	XDS	3.70×10^{-4}	
		ECVAM	3.70×10^{-4}	
		Hiyoshi	NR (3.70×10^{-5})	

^aIf no cytotoxicity was reported, the highest concentration tested is reported in parenthesis

^bAfter the initial test was conducted, the laboratory changed the testing concentrations used, in order to more adequately cover the concentration-response curve

^cLaboratory voluntarily repeated testing.

Abbreviations: ECVAM = European Centre for the Validation of Alternative Methods; Hiyoshi = Hiyoshi Corporation; M = molar; NR = Not Reported; XDS = Xenobiotic Detection Systems, Inc.

Table G3-1 Agonist Viability Summary for Phase 2a, 2b, and 3 Range Finder Experiments (Continued)

Chemical	Phase	Laboratory	Minimum Cytotoxic Concentration (M) ^{a,b,c}	
			Exp 1	Exp 2
Diethylhexyl phthalate	3	XDS	3.03×10^{-4}	
		ECVAM	3.03×10^{-3}	
		Hiyoshi	NR (3.03×10^{-5})	
Dicofol	3	XDS	2.70×10^{-4}	
		ECVAM	2.70×10^{-4}	2.70×10^{-5}
		Hiyoshi	NR (2.70×10^{-5})	
Dibenzo[<i>a,h</i>]anthracene	3	XDS	NR (3.59×10^{-5})	
		ECVAM	NR (3.59×10^{-6})	
		Hiyoshi	NR (3.59×10^{-5})	
Di-n-butyl phthalate	3	XDS	3.59×10^{-4}	
		ECVAM	3.59×10^{-3}	
		Hiyoshi	NR (3.59×10^{-4})	
Dexamethasone	3	XDS	2.55×10^{-3}	
		ECVAM	NR (2.55×10^{-3})	
		Hiyoshi	NR (2.55×10^{-5})	
Daidzein	3	XDS	3.93×10^{-4}	
		ECVAM	NR (3.93×10^{-4})	3.93×10^{-3}
		Hiyoshi	NR (3.93×10^{-4})	
Clomiphene citrate	3	XDS	1.67×10^{-5}	
		ECVAM	1.67×10^{-4}	
		Hiyoshi	1.67×10^{-5}	
Apigenin	3	XDS	3.70×10^{-4}	
		ECVAM	3.70×10^{-3}	
		Hiyoshi	NR (3.70×10^{-4})	
4- <i>tert</i> -Octylphenol	3	XDS	4.85×10^{-5}	
		ECVAM	4.85×10^{-5}	4.85×10^{-5}
		Hiyoshi	4.85×10^{-5}	
4-Hydroxytamoxifen	3	XDS	2.58×10^{-5}	
		ECVAM	2.58×10^{-6}	
		Hiyoshi	2.58×10^{-5}	

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^bAfter the initial test was conducted, the laboratory changed the testing concentrations used, in order to more adequately cover the concentration-response curve

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Table G3-1 Agonist Viability Summary for Phase 2a, 2b, and 3 Range Finder Experiments (Continued)

Chemical	Phase	Laboratory	Minimum Cytotoxic Concentration (M) ^{a,b,c}	
			Exp 1	Exp 2
4-Cumylphenol	3	XDS	4.71×10^{-4}	
		ECVAM	4.71×10^{-4}	
		Hiyoshi	4.71×10^{-4}	
2-sec-butylphenol	3	XDS	6.66×10^{-4}	
		ECVAM	6.66×10^{-4}	
		Hiyoshi	6.66×10^{-4}	
2,4,5-Tricholorophenoxy acetic acid	3	XDS	3.91×10^{-3}	
		ECVAM	NR (3.91×10^{-3})	
		Hiyoshi	3.91×10^{-3}	
17- α Estradiol	3	XDS	3.67×10^{-4}	
		ECVAM	NR (3.67×10^{-3})	
		Hiyoshi	NR (3.67×10^{-5})	
17- β Estradiol	3	XDS	3.67×10^{-4}	NR
		ECVAM	3.67×10^{-4}	(3.67×10^{-3})
		Hiyoshi	NR (3.67×10^{-5})	
Norethynodrel	3	XDS	3.35×10^{-4}	
		ECVAM	3.35×10^{-4}	
		Hiyoshi	NR (3.35×10^{-4})	
Phenobarbital	3	XDS	NR (4.31×10^{-3})	
		ECVAM	4.31×10^{-4}	
		Hiyoshi	Not Tested	
Sodium azide	3	XDS	NR (1.54×10^{-3})	
		ECVAM	NR (1.54×10^{-3})	
		Hiyoshi	NR (1.54×10^{-3})	
Testosterone	3	XDS	3.47×10^{-4}	
		ECVAM	3.47×10^{-4}	
		Hiyoshi	NR (3.47×10^{-4})	
4-Androstenedione	3	XDS	3.49×10^{-4}	
		ECVAM	3.49×10^{-5}	
		Hiyoshi	3.49×10^{-4}	

^aIf no cytotoxicity was reported, the highest concentration tested is reported in parenthesis

^bAfter the initial test was conducted, the laboratory changed the testing concentrations used, in order to more adequately cover the concentration-response curve

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Hiyoshi = Hiyoshi Corporation; M = molar; NR = Not Reported; XDS = Xenobiotic Detection Systems, Inc.

Table G3-1 Agonist Viability Summary for Phase 2a, 2b, and 3 Range Finder Experiments (Continued)

Chemical	Phase	Laboratory	Minimum Cytotoxic Concentration (M) ^{a,b,c}	
			Exp 1	Exp 2
5 α -dihydrotestosterone	3	XDS	3.44×10^{-4}	
		ECVAM	3.44×10^{-5}	
		Hiyoshi	NR (3.44×10^{-5})	
Actinomycin D	3	XDS	7.97×10^{-8}	
		ECVAM	7.97×10^{-8}	
		Hiyoshi	7.97×10^{-7}	
Coumestrol	3	XDS	3.73×10^{-4}	
		ECVAM	NR (3.73×10^{-4})	
		Hiyoshi	NR (3.73×10^{-5})	
Methyl testosterone	3	XDS	3.31×10^{-5}	
		ECVAM	3.31×10^{-5}	
		Hiyoshi	NR (3.31×10^{-4})	
Morin	3	XDS	3.31×10^{-3}	
		ECVAM	3.31×10^{-4}	
		Hiyoshi	3.31×10^{-3}	
12-O-tetradecanoyl-phorbol-13-acetate	3	XDS	1.62×10^{-5}	
		ECVAM	1.62×10^{-5}	
		Hiyoshi	1.62×10^{-5}	

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^bAfter the initial test was conducted, the laboratory changed the testing concentrations used, in order to more adequately cover the concentration-response curve

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Table G3-2 Antagonist Viability Summary for Phase 2a, 2b, and 3 Range Finder Experiments

Chemical	Phase	Laboratory	Minimum Cytotoxic Concentration (M) ^{a,b,c}	
			Exp 1	Exp 2
Dibenzof[<i>a,h</i>] anthracene	2a	XDS	3.59×10^{-5}	
		ECVAM	3.59×10^{-5}	
		Hiyoshi	NR (3.59×10^{-5})	
Progesterone	2a	XDS	3.18×10^{-4}	
		ECVAM	3.18×10^{-4}	
		Hiyoshi	NR (3.18×10^{-5})	
<i>p-n</i> -nonylphenol	2a	XDS	4.54×10^{-5}	
		ECVAM	4.54×10^{-4}	
		Hiyoshi	4.54×10^{-5}	
Tamoxifen	2a	XDS	2.69×10^{-5}	
		ECVAM	2.69×10^{-5}	
		Hiyoshi	2.69×10^{-5}	
Apigenin	2b	XDS	3.70×10^{-5}	
		ECVAM	NR (3.70×10^{-5})	
		Hiyoshi	NR (3.70×10^{-5})	
Atrazine	2b	XDS	NR (4.64×10^{-4})	
		ECVAM	NR (4.64×10^{-4})	
		Hiyoshi	NR (4.64×10^{-4})	
Butylbenzyl phthalate	2b	XDS	3.20×10^{-4}	
		ECVAM	NR (3.20×10^{-5})	
		Hiyoshi	NR (3.20×10^{-5})	
Corticosterone	2b	XDS	2.89×10^{-3}	
		ECVAM	2.89×10^{-3}	
		Hiyoshi	NR (2.89×10^{-4})	
<i>o,p'</i> -DDT	2b	XDS	2.82×10^{-4}	
		ECVAM	NR (2.82×10^{-5})	
		Hiyoshi	NR (2.82×10^{-5})	

^aIf no cytotoxicity was reported, the highest concentration tested is reported in parenthesis

^bAfter the initial test was conducted, the laboratory changed the testing concentrations used, in order to more adequately cover the concentration-response curve

^cLaboratory voluntarily repeated testing.

Abbreviations: ECVAM = European Centre for the Validation of Alternative Methods; Hiyoshi = Hiyoshi Corporation; M = molar; NR = Not Reported; XDS = Xenobiotic Detection Systems, Inc.

Table G3-2 Antagonist Viability Summary for Phase 2a, 2b, and 3 Range Finder Experiments (Continued)

Chemical	Phase	Laboratory	Minimum Cytotoxic Concentration (M) ^{a,b,c}	
			Exp 1	Exp 2
Flavone	2b	XDS	4.50×10^{-4}	
		ECVAM	4.50×10^{-4}	
		Hiyoshi	NR (4.50×10^{-5})	
Genistein	2b	XDS	3.70×10^{-4}	
		ECVAM	NR (3.70×10^{-4})	
		Hiyoshi	NR (3.70×10^{-5})	
Resveratrol	2b	XDS	4.38×10^{-4}	
		ECVAM	NR (4.38×10^{-4})	
		Hiyoshi	NR (4.38×10^{-4})	
Actinomycin D	3	XDS	7.97×10^{-8}	
		ECVAM	7.97×10^{-8}	
		Hiyoshi	7.97×10^{-8}	
Bisphenol A	3	XDS	4.38×10^{-4}	
		ECVAM	4.38×10^{-4}	
		Hiyoshi	4.38×10^{-4}	
Bisphenol B	3	XDS	4.13×10^{-4}	
		ECVAM	4.13×10^{-4}	4.13×10^{-4}
		Hiyoshi	4.13×10^{-4}	
Diethylstilbestrol	3	XDS	3.73×10^{-10}	3.73×10^{-4}
		ECVAM	NR (3.73×10^{-4})	
		Hiyoshi	NR (3.73×10^{-5})	
17- α Ethynodiol diacetate	3	XDS	3.37×10^{-4}	
		ECVAM	NR (3.37×10^{-5})	3.37×10^{-4}
		Hiyoshi	NR (3.37×10^{-5})	
4-Androstenedione	3	XDS	3.49×10^{-10}	
		ECVAM	3.49×10^{-4}	
		Hiyoshi	3.49×10^{-4}	

^aIf no cytotoxicity was reported, the highest concentration tested is reported in parenthesis

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^cLaboratory voluntarily repeated testing.

Abbreviations: ECVAM = European Centre for the Validation of Alternative Methods; Hiyoshi = Hiyoshi Corporation; M = molar; NR = Not Reported; XDS = Xenobiotic Detection Systems, Inc.

**Table G3-2 Antagonist Viability Summary for Phase 2a, 2b, and 3
Range Finder Experiments (Continued)**

Clomiphene citrate	3	XDS	1.67×10^{-5}	1.67×10^{-4}
		ECVAM	1.67×10^{-4}	
		Hiyoshi	NR (1.67×10^{-5})	
Coumestrol	3	XDS	3.73×10^{-4}	4.71×10^{-4}
		ECVAM	NR (3.73×10^{-4})	
		Hiyoshi	NR (3.73×10^{-5})	
4-Cumylphenol	3	XDS	4.71×10^{-4}	4.71×10^{-4}
		ECVAM	4.71×10^{-4}	
		Hiyoshi	NR (4.71×10^{-5})	
Daidzein	3	XDS	NR (3.93×10^{-4})	3.93×10^{-4}
		ECVAM	NR (3.93×10^{-4})	
		Hiyoshi	NR (3.93×10^{-5})	
Di - n -butyl phthalate	3	XDS	3.59×10^{-4}	3.14×10^{-9}
		ECVAM	3.59×10^{-3}	
		Hiyoshi	NR (3.59×10^{-5})	
<i>p,p'</i> -DDE	3	XDS	NR (3.14×10^{-5})	3.14×10^{-9}
		ECVAM	3.14×10^{-4}	
		Hiyoshi	NR (3.14×10^{-5})	
Diethylhexyl phthalate	3	XDS	3.03×10^{-4}	2.55×10^{-4}
		ECVAM	NR (3.03×10^{-3})	
		Hiyoshi	NR (3.03×10^{-5})	
Dexamethasone	3	XDS	2.55×10^{-4}	NR (2.55×10^{-4})
		ECVAM	NR (2.55×10^{-4})	
		Hiyoshi	NR (2.55×10^{-4})	
5α -Dihydrotestosterone	3	XDS	3.44×10^{-4}	NR (3.44×10^{-4})
		ECVAM	3.44×10^{-4}	
		Hiyoshi	NR (3.44×10^{-5})	

^aIf no cytotoxicity was reported, the highest concentration tested is reported in parenthesis

^bAfter the initial test was conducted, the laboratory changed the testing concentrations used, in order to more adequately cover the concentration-response curve

^cLaboratory voluntarily repeated testing.

Abbreviations: ECVAM = European Centre for the Validation of Alternative Methods; Hiyoshi = Hiyoshi Corporation; M = molar; NR = Not Reported; XDS = Xenobiotic Detection Systems, Inc.

Table G3-2 Antagonist Viability Summary for Phase 2a, 2b, and 3 Range Finder Experiments (Continued)

Chemical	Phase	Laboratory	Minimum Cytotoxic Concentration (M) ^{a,b,c}	
			Exp 1	Exp 2
Dicofol	3	XDS	2.70×10^{-5}	
		ECVAM	2.70×10^{-5}	2.70×10^{-4}
		Hiyoshi	NR (2.70×10^{-5})	
17- α Estradiol	3	XDS	NR (3.67×10^{-5})	3.67×10^{-5}
		ECVAM	NR (3.67×10^{-4})	
		Hiyoshi	NR (3.67×10^{-5})	
17- β Estradiol	3	XDS	NR (3.67×10^{-5})	3.67×10^{-5}
		ECVAM	NR (3.67×10^{-4})	NR (3.67×10^{-3})
		Hiyoshi	NR (3.67×10^{-5})	
Ethyl paraben	3	XDS	6.02×10^{-3}	
		ECVAM	6.02×10^{-3}	
		Hiyoshi	6.02×10^{-3}	
Estrone	3	XDS	NR (3.70×10^{-5})	3.70×10^{-5}
		ECVAM	NR (3.70×10^{-5})	
		Hiyoshi	NR (3.70×10^{-5})	
Fluoranthene	3	XDS	NR (4.94×10^{-5})	4.94×10^{-4}
		ECVAM	NR (4.94×10^{-4})	
		Hiyoshi	NR (4.94×10^{-5})	
<i>meso</i> -Hexestrol	3	XDS	3.70×10^{-4}	
		ECVAM	3.70×10^{-5}	
		Hiyoshi	NR (3.70×10^{-5})	

^aIf no cytotoxicity was reported, the highest concentration tested is reported in parenthesis

^bAfter the initial test was conducted, the laboratory changed the testing concentrations used, in order to more adequately cover the concentration-response curve

^cLaboratory voluntarily repeated testing.

Abbreviations: ECVAM = European Centre for the Validation of Alternative Methods; Hiyoshi = Hiyoshi Corporation; M = molar; NR = Not Reported; XDS = Xenobiotic Detection Systems, Inc.

**Table G3-2 Antagonist Viability Summary for Phase 2a, 2b, and 3
Range Finder Experiments (Continued)**

Chemical	Phase	Laboratory	Minimum Cytotoxic Concentration (M) ^{a,b,c}	
			Exp 1	Exp 2
Hydroxyflutamide	3	XDS	3.42×10^{-5}	
		ECVAM	NR (3.42×10^{-4})	3.42×10^{-3}
		Hiyoshi	NR (3.42×10^{-4})	
Kepone	3	XDS	2.04×10^{-4}	
		ECVAM	2.04×10^{-4}	
		Hiyoshi	NR (2.04×10^{-5})	
Kaempferol	3	XDS	3.49×10^{-4}	
		ECVAM	NR (3.49×10^{-4})	
		Hiyoshi	NR (3.49×10^{-5})	
<i>p,p'</i> - Methoxychlor	3	XDS	2.89×10^{-5}	
		ECVAM	NR (2.89×10^{-4})	2.89×10^{-3}
		Hiyoshi	NR (2.89×10^{-5})	
Morin	3	XDS	3.31×10^{-3}	
		ECVAM	3.31×10^{-4}	
		Hiyoshi	NR (3.31×10^{-4})	
Methyl testosterone	3	XDS	3.31×10^{-5}	
		ECVAM	3.31×10^{-5}	
		Hiyoshi	3.31×10^{-4}	
Norethynodrel	3	XDS	3.35×10^{-4}	
		ECVAM	3.35×10^{-4}	
		Hiyoshi	NR (3.35×10^{-5})	
4- <i>tert</i> -Octylphenol	3	XDS	4.85×10^{-4}	
		ECVAM	4.85×10^{-5}	4.85×10^{-5}
		Hiyoshi	NR (4.85×10^{-5})	
4-Hydroxy-tamoxifen	3	XDS	2.58×10^{-5}	
		ECVAM	2.58×10^{-4}	
		Hiyoshi	2.58×10^{-5}	

^aIf no cytotoxicity was reported, the highest concentration tested is reported in parenthesis

^bAfter the initial test was conducted, the laboratory changed the testing concentrations used, in order to more adequately cover the concentration-response curve

^cLaboratory voluntarily repeated testing.

Abbreviations: ECVAM = European Centre for the Validation of Alternative Methods; Hiyoshi = Hiyoshi Corporation; M = molar; NR = Not Reported; XDS = Xenobiotic Detection Systems, Inc.

Table G3-2 Antagonist Viability Summary for Phase 2a, 2b, and 3 Range Finder Experiments (Continued)

Chemical	Phase	Laboratory	Minimum Cytotoxic Concentration (M) ^{a,b,c}	
			Exp 1	Exp 2
Phenobarbital	3	XDS	NR (4.31 × 10 ⁻³)	
		ECVAM	NR (4.31 × 10 ⁻³)	
		Hiyoshi	Not Tested	
Phenolphthalein	3	XDS	3.12 × 10 ⁻³	
		ECVAM	3.12 × 10 ⁻³	
		Hiyoshi	3.12 × 10 ⁻³	
Propylthiouracil	3	XDS	NR (5.87 × 10 ⁻⁴)	5.87 × 10 ⁻³
		ECVAM	5.87 × 10 ⁻³	
		Hiyoshi	NR (5.87 × 10 ⁻⁴)	
Raloxifene HCl	3	XDS	1.96 × 10 ⁻⁵	
		ECVAM	1.96 × 10 ⁻⁴	
		Hiyoshi	NR (1.96 × 10 ⁻⁵)	
Sodium azide	3	XDS	NR (1.54 × 10 ⁻³)	
		ECVAM	NR (1.54 × 10 ⁻³)	
		Hiyoshi	NR (1.54 × 10 ⁻³)	
2-sec-Butylphenol	3	XDS	6.66 × 10 ⁻⁵	
		ECVAM	6.66 × 10 ⁻⁴	
		Hiyoshi	6.66 × 10 ⁻⁴	
2,4,5-Trichlorophenoxyacetic acid	3	XDS	NR (3.91 × 10 ⁻³)	
		ECVAM	3.91 × 10 ⁻⁵	
		Hiyoshi	3.91 × 10 ⁻³	
Testosterone	3	XDS	3.47 × 10 ⁻⁴	
		ECVAM	3.47 × 10 ⁻³	
		Hiyoshi	3.47 × 10 ⁻⁴	
12 - O - Tetradecanoylphorbol-13-acetate	3	XDS	1.62 × 10 ⁻⁵	
		ECVAM	1.62 × 10 ⁻⁴	
		Hiyoshi	NR (1.62 × 10 ⁻⁵)	
Vinclozolin	3	XDS	3.50 × 10 ⁻⁴	
		ECVAM	NR (3.50 × 10 ⁻⁴)	
		Hiyoshi	NR (3.50 × 10 ⁻⁵)	

^aIf no cytotoxicity was reported, the highest concentration tested is reported in parenthesis

^bAfter the initial test was conducted, the laboratory changed the testing concentrations used, in order to more adequately cover the concentration-response curve

^cLaboratory voluntarily repeated testing.

Abbreviations: ECVAM = European Centre for the Validation of Alternative Methods; Hiyoshi = Hiyoshi Corporation; M = molar; NR = Not Reported; XDS = Xenobiotic Detection Systems, Inc.

Table G3-3 Viability Summary for Phase 4 Range Finder Experiments

Chemical	AGONIST ^{a,b,c}		ANTAGONIST ^{a,b,c}	
	EXP #1	EXP #2	EXP #1	EXP #2
17 β -Trenbolone	3.70×10^{-4}		3.70×10^{-4}	
19-Nortestosterone	NR (3.64×10^{-3})		3.64×10^{-4}	
4-hydroxyandrostenedione	3.31×10^{-3}		3.31×10^{-4}	
Ammonium perchlorate	8.51×10^{-3}		8.51×10^{-3}	
Apomorphine	3.74×10^{-3}		3.74×10^{-5}	
Bicalutamide	2.32×10^{-4}		2.32×10^{-4}	
Chrysin	3.93×10^{-3}		3.93×10^{-5}	
Cycloheximide	3.55×10^{-6}		3.55×10^{-5}	
Cyproterone acetate	2.40×10^{-4}		2.4×10^{-9}	2.40×10^{-4}
Fenarimol	3.02×10^{-4}		3.02×10^{-7}	
Finasteride	2.68×10^{-5}		2.68×10^{-4}	
Fluoxymestrone	2.97×10^{-4}	2.97×10^{-4}	2.97×10^{-4}	
Flutamide	3.62×10^{-4}	3.62×10^{-3}	3.62×10^{-4}	
Haloperidol	2.66×10^{-7}		2.66×10^{-7}	
Ketoconazole	NR (9.41×10^{-5})		1.88×10^{-5}	
L-Thyroxine	1.29×10^{-4}		1.29×10^{-4}	
Linuron	4.01×10^{-5}		4.01×10^{-3}	
Medroxyprogesterone acetate	2.59×10^{-4}		NR (2.59×10^{-5})	
Mifepristone	2.33×10^{-5}		2.33×10^{-5}	
Nilutamide	3.15×10^{-3}		3.15×10^{-3}	
Oxazepam	3.49×10^{-6}		3.49×10^{-4}	
Pimozide	2.17×10^{-4}		2.17×10^{-5}	
Procymidone	3.52×10^{-4}		3.52×10^{-4}	
Reserpine	1.64×10^{-5}		1.64×10^{-5}	
Spiromolactone	2.40×10^{-5}		2.40×10^{-4}	

^aIf no cytotoxicity was reported, the highest concentration tested is reported in parenthesis^bAfter the initial test was conducted, the laboratory changed the testing concentrations used, in order to more adequately cover the concentration-response curve^cLaboratory voluntarily repeated testing.

Abbreviations: ECVAM = European Centre for the Validation of Alternative Methods; Hiyoshi = Hiyoshi Corporation; M = molar; NR = Not Reported; XDS = Xenobiotic Detection Systems, Inc.

Table G3-? Agonist Viability Summary for Phase 2a, 2b, and 3 Comprehensive Experiments

Chemical	Phase	Laboratory	Minimum Cytotoxic Concentration (M) ^{a,b,c}			
			Exp 1	Exp 2	Exp 3	Exp 4
Bisphenol A	2a	XDS	8.76×10^{-5}	4.38×10^{-4}	4.38×10^{-4}	
		ECVAM	NR (4.38×10^{-5})	NR (4.38×10^{-5})	NR (4.38×10^{-5})	
		Hiyoshi	NR (4.38×10^{-5})	NR (4.38×10^{-5})	NR (4.38×10^{-5})	
Bisphenol B	2a	XDS	8.25×10^{-5}	8.25×10^{-5}	8.25×10^{-5}	
		ECVAM	4.13×10^{-5}	4.13×10^{-5}	NR (4.13×10^{-5})	
		Hiyoshi	NR (4.13×10^{-5})	NR (4.13×10^{-5})	1.03×10^{-5}	
Corticosterone	2a	XDS	NR (2.89×10^{-5})	NR (2.89×10^{-5})	NR (2.89×10^{-5})	
		ECVAM	1.44×10^{-3}	1.44×10^{-3}	1.44×10^{-3}	
		Hiyoshi	7.22×10^{-4}	1.44×10^{-3}	1.44×10^{-3}	
Diethylstilbestrol	2a	XDS	3.73×10^{-10}	NR (3.73×10^{-7})	3.73×10^{-7}	
		ECVAM	NR (3.73×10^{-7})	3.73×10^{-7}	NR (3.73×10^{-7})	
		Hiyoshi	NR (3.73×10^{-6})	NR (3.73×10^{-6})	NR (3.73×10^{-6})	
Atrazine	2b	XDS	NR (4.64×10^{-4})	4.64×10^{-4}	4.64×10^{-4}	
		ECVAM	NR (4.64×10^{-4})	NR (4.64×10^{-4})	NR (4.64×10^{-4})	
		Hiyoshi	NR (4.64×10^{-4})	NR (4.64×10^{-4})	NR (4.64×10^{-4})	
Butylbenzyl phthalate	2b	XDS	3.20×10^{-4}	6.40×10^{-5}	3.20×10^{-4}	
		ECVAM	NR (3.20×10^{-5})	NR (3.20×10^{-5})	NR (3.20×10^{-5})	
		Hiyoshi	NR (3.20×10^{-5})	NR (3.20×10^{-5})	NR (3.20×10^{-5})	
<i>o,p'</i> -DDT	2b	XDS	5.64×10^{-6}	2.82×10^{-5}	2.82×10^{-5}	
		ECVAM	NR (2.82×10^{-5})	NR (2.82×10^{-5})	NR (2.82×10^{-5})	
		Hiyoshi	NR (2.82×10^{-5})	NR (2.82×10^{-5})	NR (2.82×10^{-5})	
17- α Ethinyl estradiol	2b	XDS	3.37×10^{-5}	3.37×10^{-7}	3.37×10^{-7}	3.37×10^{-7}
		ECVAM	NR (3.37×10^{-9})	NR (3.37×10^{-9})	NR (3.37×10^{-9})	
		Hiyoshi	NR (3.37×10^{-10})	NR (3.37×10^{-10})	NR (3.37×10^{-10})	
Flavone	2b	XDS	2.25×10^{-4}	2.25×10^{-4}	2.25×10^{-4}	
		ECVAM	4.50×10^{-4}	4.50×10^{-4}	4.50×10^{-4}	
		Hiyoshi	NR (4.50×10^{-4})	NR (4.50×10^{-4})	NR (4.50×10^{-4})	

^aIf no cytotoxicity was reported, the highest concentration tested is reported in parenthesis^bAfter the initial test was conducted, the laboratory changed the testing concentrations used, in order to more adequately cover the concentration-response curve^cLaboratory voluntarily repeated testing.

Abbreviations: ECVAM = European Centre for the Validation of Alternative Methods; Hiyoshi = Hiyoshi Corporation; M = molar; NR = Not Reported; XDS = Xenobiotic Detection Systems, Inc.

Table G3-? Agonist Viability Summary for Phase 2a, 2b, and 3 Comprehensive Experiments (Continued)

Chemical	Phase	Laboratory	Minimum Cytotoxic Concentration (M) ^{a,b,c}			
			Exp 1	Exp 2	Exp 3	Exp 4
Genistein	2b	XDS	3.70×10^{-4}	3.70×10^{-4}	7.50×10^{-5}	
		ECVAM	NR (3.70×10^{-5})	NR (3.70×10^{-5})	NR (3.70×10^{-5})	
		Hiyoshi	NR (3.70×10^{-4})	NR (3.70×10^{-4})	NR (3.70×10^{-4})	NR (3.70×10^{-4})
<i>p</i> -n-nonylphenol	2b	XDS	9.08×10^{-6}	9.08×10^{-6}	4.54×10^{-5}	
		ECVAM	NR (4.54×10^{-5})	NR (4.54×10^{-5})	4.54×10^{-5}	
		Hiyoshi	5.67×10^{-5}	5.67×10^{-5}	5.67×10^{-5}	
Vinclozolin	2b	XDS	6.99×10^{-6}	6.99×10^{-6}	3.50×10^{-5}	
		ECVAM	NR (3.50×10^{-5})	NR (3.50×10^{-5})	NR (3.50×10^{-5})	
		Hiyoshi	NR (3.50×10^{-4})	NR (3.50×10^{-4})	NR (3.50×10^{-4})	NR (3.50×10^{-4})
Actinomycin D	3	XDS	7.78×10^{-11}			
		ECVAM	NR (7.97×10^{-9})			
		Hiyoshi	3.11×10^{-7}			
4-Androstenedione	3	XDS	NR (3.49×10^{-4})			
		ECVAM	NR (3.49×10^{-6})			
		Hiyoshi	NR (3.49×10^{-4})			
Apigenin	3	XDS	3.70×10^{-4}			
		ECVAM	1.48×10^{-4}	1.48×10^{-4}	1.48×10^{-4}	
		Hiyoshi	NR (3.70×10^{-5})			
Clomiphene citrate	3	XDS	NR (1.67×10^{-7})			
		ECVAM	1.67×10^{-5}			
		Hiyoshi	1.67×10^{-5}			
Coumestrol	3	XDS	1.49×10^{-5}	NR (3.73×10^{-8})		
		ECVAM	NR (3.73×10^{-4})			
		Hiyoshi	NR (3.73×10^{-5})			
4-Cumylphenol	3	XDS	NR (4.71×10^{-5})			
		ECVAM	4.71×10^{-5}			
		Hiyoshi	NR (4.71×10^{-5})			

^aIf no cytotoxicity was reported, the highest concentration tested is reported in parenthesis

^bAfter the initial test was conducted, the laboratory changed the testing concentrations used, in order to more adequately cover the concentration-response curve

^cLaboratory voluntarily repeated testing.

Abbreviations: ECVAM = European Centre for the Validation of Alternative Methods; Hiyoshi = Hiyoshi Corporation; M = molar; NR = Not Reported; XDS = Xenobiotic Detection Systems, Inc.

Table G3-? Agonist Viability Summary for Phase 2a, 2b, and 3 Comprehensive Experiments (Continued)

Chemical	Phase	Laboratory	Minimum Cytotoxic Concentration (M) ^{a,b,c}			
			Exp 1	Exp 2	Exp 3	Exp 4
Daidzein	3	XDS	3.93×10^{-4}			
		ECVAM	NR (3.93×10^{-4})			
		Hiyoshi	NR (3.93×10^{-5})			
Dibenzo[<i>a,h</i>]anthracene	3	XDS	3.95×10^{-5}			
		ECVAM	NR (3.95×10^{-6})			
		Hiyoshi	NR (3.95×10^{-10})	3.95×10^{-5}		
Di - <i>n</i> -butyl phthalate	3	XDS	NR (3.59×10^{-4})			
		ECVAM	3.59×10^{-4}			
		Hiyoshi	3.59×10^{-4}	NR (3.59×10^{-4})		
<i>p,p'</i> -DDE	3	XDS	1.57×10^{-4}	NR (3.14×10^{-6})		
		ECVAM	1.97×10^{-4}			
		Hiyoshi	3.14×10^{-4}			
Diethylhexyl phthalate	3	XDS	NR (3.03×10^{-3})			
		ECVAM	NR (3.03×10^{-3})			
		Hiyoshi	1.51×10^{-3}			
Dexamethasone	3	XDS	NR (2.55×10^{-4})			
		ECVAM	1.27×10^{-3}			
		Hiyoshi	NR (2.55×10^{-5})			
5α -Dihydrotestosterone	3	XDS	6.89×10^{-5}			
		ECVAM	NR (3.44×10^{-8})			
		Hiyoshi	3.44×10^{-5}	3.44×10^{-6}		
Dicofol	3	XDS	6.75×10^{-5}			
		ECVAM	1.35×10^{-4}			
		Hiyoshi	3.37×10^{-4}			
17- α Estradiol	3	XDS	NR (3.67×10^{-7})			
		ECVAM	NR (3.67×10^{-7})	NR (3.67×10^{-7})	NR (3.67×10^{-7})	
		Hiyoshi	NR (3.67×10^{-8})			

^aIf no cytotoxicity was reported, the highest concentration tested is reported in parenthesis

^bAfter the initial test was conducted, the laboratory changed the testing concentrations used, in order to more adequately cover the concentration-response curve

^cLaboratory voluntarily repeated testing.

Abbreviations: ECVAM = European Centre for the Validation of Alternative Methods; Hiyoshi = Hiyoshi Corporation; M = molar; NR = Not Reported; XDS = Xenobiotic Detection Systems, Inc.

Table G3-? Agonist Viability Summary for Phase 2a, 2b, and 3 Comprehensive Experiments (Continued)

Chemical	Phase	Laboratory	Minimum Cytotoxic Concentration (M) ^{a,b,c}			
			Exp 1	Exp 2	Exp 3	Exp 4
17-β Estradiol	3	XDS	NR (3.67×10^{-7})			
		ECVAM	NR (3.67×10^{-7})			
		Hiyoshi	NR (3.67×10^{-10})			
Ethyl paraben	3	XDS	NR (6.02×10^{-4})			
		ECVAM	NR (6.02×10^{-4})			
		Hiyoshi	NR (6.02×10^{-5})	NR (6.02×10^{-4})		
Estrone	3	XDS	NR (3.70×10^{-6})			
		ECVAM	NR (3.70×10^{-8})			
		Hiyoshi	NR (3.70×10^{-6})	NR (3.70×10^{-9})		
Fluoranthene	3	XDS	4.94×10^{-4}			
		ECVAM	NR (4.94×10^{-5})			
		Hiyoshi	1.98×10^{-4}			
<i>meso</i> -Hexestrol	3	XDS	NR (3.70×10^{-7})			
		ECVAM	NR (3.70×10^{-8})			
		Hiyoshi	NR (3.70×10^{-9})	NR (3.70×10^{-9})		
Hydroxyflutamide	3	XDS	NR (3.42×10^{-4})	NR (3.42×10^{-9})		
		ECVAM	NR (3.42×10^{-4})			
		Hiyoshi	NR (3.42×10^{-4})			
Kepone	3	XDS	2.04×10^{-5}			
		ECVAM	NR (2.04×10^{-5})			
		Hiyoshi	2.04×10^{-5}			

^aIf no cytotoxicity was reported, the highest concentration tested is reported in parenthesis.

^bAfter the initial test was conducted, the laboratory changed the testing concentrations used, in order to more adequately cover the concentration-response curve.

^cLaboratory voluntarily repeated testing.

Abbreviations: ECVAM = European Centre for the Validation of Alternative Methods; Hiyoshi = Hiyoshi Corporation; M = molar; NR = Not Reported; XDS = Xenobiotic Detection Systems, Inc.

Table G3-? Agonist Viability Summary for Phase 2a, 2b, and 3 Comprehensive Experiments (Continued)

Chemical	Phase	Laboratory	Minimum Cytotoxic Concentration (M) ^{a,b,c}			
			Exp 1	Exp 2	Exp 3	Exp 4
Kaempferol	3	XDS	3.49×10^{-4}			
		ECVAM	NR (3.49×10^{-5})			
		Hiyoshi	NR (3.49×10^{-5})			
<i>p,p'</i> - Methoxychlor	3	XDS	NR (2.89×10^{-4})	NR (2.89×10^{-4})		
		ECVAM	NR (2.89×10^{-5})			
		Hiyoshi	NR (2.89×10^{-3})	1.16×10^{-4}		
Morin	3	XDS	3.31×10^{-3}	NR (3.31×10^{-4})		
		ECVAM	NR (3.31×10^{-4})			
		Hiyoshi	3.31×10^{-3}			
Methyl testosterone	3	XDS	6.61×10^{-5}	NR (3.31×10^{-5})	NR (3.31×10^{-5})	
		ECVAM	NR (3.31×10^{-6})			
		Hiyoshi	NR (3.31×10^{-4})	NR (3.31×10^{-5})		
Norethynodrel	3	XDS	NR (3.35×10^{-7})	NR (3.35×10^{-5})		
		ECVAM	NR (3.35×10^{-7})			
		Hiyoshi	NR (3.35×10^{-6})	NR (3.35×10^{-8})		
4- <i>tert</i> -Octylphenol	3	XDS	NR (4.85×10^{-7})			
		ECVAM	4.85×10^{-6}			
		Hiyoshi	2.42×10^{-5}	NR (4.85×10^{-6})		
4-Hydroxy-tamoxifen	3	XDS	NR (2.69×10^{-8})			
		ECVAM	2.69×10^{-6}			
		Hiyoshi	1.35×10^{-5}	2.69×10^{-6}		
Phenobarbital	3	XDS	4.31×10^{-3}	NR (4.31×10^{-4})		
		ECVAM	NR (4.31×10^{-5})			
		Hiyoshi	Not Tested			

^aIf no cytotoxicity was reported, the highest concentration tested is reported in parenthesis

^bAfter the initial test was conducted, the laboratory changed the testing concentrations used, in order to more adequately cover the concentration-response curve

^cLaboratory voluntarily repeated testing.

Abbreviations: ECVAM = European Centre for the Validation of Alternative Methods; Hiyoshi = Hiyoshi Corporation; M = molar; NR = Not Reported; XDS = Xenobiotic Detection Systems, Inc.

Table G3-? Agonist Viability Summary for Phase 2a, 2b, and 3 Comprehensive Experiments (Continued)

Chemical	Phase	Laboratory	Minimum Cytotoxic Concentration (M) ^{a,b,c}			
			Exp 1	Exp 2	Exp 3	Exp 4
Phenolphthalin	3	XDS	NR (3.12×10^{-3})			
		ECVAM	3.12×10^{-3}			
		Hiyoshi	NR (3.12×10^{-3})	3.12×10^{-3}		
Progesterone	3	XDS	NR (3.18×10^{-5})	NR (3.18×10^{-5})		
		ECVAM	NR (3.18×10^{-5})			
		Hiyoshi	NR (3.18×10^{-6})	3.18×10^{-4}		
Propylthiouracil	3	XDS	NR (5.87×10^{-3})	NR (5.87×10^{-3})		
		ECVAM	5.87×10^{-3}			
		Hiyoshi	NR (5.87×10^{-3})			
Raloxifene HCl	3	XDS	2.45×10^{-5}			
		ECVAM	4.90×10^{-5}			
		Hiyoshi	NR (1.96×10^{-3})	3.06×10^{-5}		
Resveratrol	3	XDS	4.38×10^{-4}			
		ECVAM	4.38×10^{-4}			
		Hiyoshi	NR (4.38×10^{-9})	NR (4.38×10^{-6})	NR (4.38×10^{-6})	
Sodium azide	3	XDS	NR (1.54×10^{-3})	NR (1.54×10^{-4})	NR (1.54×10^{-4})	
		ECVAM	NR (1.54×10^{-3})			
		Hiyoshi	NR (1.54×10^{-3})			
2-sec-Butylphenol	3	XDS	NR (6.66×10^{-7})			
		ECVAM	NR (6.66×10^{-6})			
		Hiyoshi	6.66×10^{-4}	6.66×10^{-4}		
Tamoxifen	3	XDS	NR (2.69×10^{-8})			
		ECVAM	2.69×10^{-6}			
		Hiyoshi	1.35×10^{-5}	2.69×10^{-5}		

^aIf no cytotoxicity was reported, the highest concentration tested is reported in parenthesis

^bAfter the initial test was conducted, the laboratory changed the testing concentrations used, in order to more adequately cover the concentration-response curve

^cLaboratory voluntarily repeated testing.

Abbreviations: ECVAM = European Centre for the Validation of Alternative Methods; Hiyoshi = Hiyoshi Corporation; M = molar; NR = Not Reported; XDS = Xenobiotic Detection Systems, Inc.

Table G3-? Agonist Viability Summary for Phase 2a, 2b, and 3 Comprehensive Experiments (Continued)

Chemical	Phase	Laboratory	Minimum Cytotoxic Concentration (M) ^{a,b,c}			
			Exp 1	Exp 2	Exp 3	Exp 4
2,4,5-Trichloro-phenoxyacetic acid	3	XDS	NR (3.91×10^{-5})			
		ECVAM	3.91×10^{-3}			
		Hiyoshi	NR (3.91×10^{-3})	3.91×10^{-3}		
Testosterone	3	XDS	6.93×10^{-5}	NR (3.47×10^{-4})		
		ECVAM	NR (3.47×10^{-8})			
		Hiyoshi	NR (3.47×10^{-4})	NR (3.47×10^{-5})		
12 - O - Tetradecanoylphorbol-13-acetate	3	XDS	NR (1.62×10^{-6})	NR (1.62×10^{-6})		
		ECVAM	1.62×10^{-6}			
		Hiyoshi	1.30×10^{-5}			

^aIf no cytotoxicity was reported, the highest concentration tested is reported in parenthesis

^bAfter the initial test was conducted, the laboratory changed the testing concentrations used, in order to more adequately cover the concentration-response curve

^cLaboratory voluntarily repeated testing.

Abbreviations: ECVAM = European Centre for the Validation of Alternative Methods; Hiyoshi = Hiyoshi Corporation; M = molar; NR = Not Reported; XDS = Xenobiotic Detection Systems, Inc.

Table G3-? Antagonist Viability Summary for Phase 2a, 2b, and 3 Comprehensive Experiments

Chemical	Phase	Laboratory	Minimum Cytotoxic Concentration (M) ^{a,b,c}			
			Exp 1	Exp 2	Exp 3	Exp 4
Dibenzof[<i>a,h</i>] anthracene	2a	XDS	3.59×10^{-6}	3.59×10^{-6}	NR (3.59×10^{-6})	
		ECVAM	NR (3.59×10^{-6})	NR (3.59×10^{-6})	NR (3.59×10^{-6})	
		Hiyoshi	NR (3.59×10^{-6})	NR (3.59×10^{-6})	NR (3.59×10^{-6})	
Progesterone	2a	XDS	1.59×10^{-4}	1.59×10^{-4}	1.59×10^{-4}	
		ECVAM	1.59×10^{-4}	1.59×10^{-4}	1.59×10^{-4}	
		Hiyoshi	NR (3.18×10^{-5})	NR (3.18×10^{-5})	NR (3.18×10^{-5})	
<i>p</i> - <i>n</i> -nonylphenol	2a	XDS	4.54×10^{-5}	9.08×10^{-6}	4.54×10^{-5}	
		ECVAM	1.13×10^{-4}	1.13×10^{-4}	1.13×10^{-4}	
		Hiyoshi	NR (4.54×10^{-5})	NR (4.54×10^{-5})	NR (4.54×10^{-5})	
Tamoxifen	2a	XDS	2.69×10^{-5}	2.69×10^{-5}	NR (2.69×10^{-5})	NR (2.69×10^{-5})
		ECVAM	2.69×10^{-5}	2.69×10^{-5}	NR (2.69×10^{-5})	
		Hiyoshi	2.69×10^{-5}	2.69×10^{-5}	2.69×10^{-5}	
Apigenin	2b	XDS	3.70×10^{-5}	NR (3.70×10^{-5})	NR (3.70×10^{-5})	
		ECVAM	NR (3.70×10^{-5})	NR (3.70×10^{-5})	NR (3.70×10^{-5})	
		Hiyoshi	NR (3.70×10^{-5})	NR (3.70×10^{-5})	NR (3.70×10^{-5})	
Atrazine	2b	XDS	NR (4.64×10^{-4})	4.64×10^{-4}	4.64×10^{-4}	
		ECVAM	NR (4.64×10^{-4})	NR (4.64×10^{-4})	NR (4.64×10^{-4})	
		Hiyoshi	NR (4.64×10^{-4})	NR (4.64×10^{-4})	NR (4.64×10^{-4})	
Butylbenzyl phthalate	2b	XDS	3.20×10^{-4}	1.60×10^{-4}	3.20×10^{-4}	
		ECVAM	NR (3.20×10^{-5})	NR (3.20×10^{-5})	NR (3.20×10^{-5})	
		Hiyoshi	NR (3.20×10^{-5})	NR (3.20×10^{-5})	NR (3.20×10^{-5})	
Corticosterone	2b	XDS	7.22×10^{-4}	7.22×10^{-4}	7.22×10^{-4}	
		ECVAM	2.89×10^{-3}	2.89×10^{-3}	2.89×10^{-3}	
		Hiyoshi	2.89×10^{-4}	2.89×10^{-4}	2.89×10^{-4}	
<i>o,p'</i> -DDT	2b	XDS	2.82×10^{-4}	2.82×10^{-4}	2.82×10^{-4}	
		ECVAM	NR (2.82×10^{-5})	NR (2.82×10^{-5})	NR (2.82×10^{-5})	
		Hiyoshi	NR (2.82×10^{-5})	NR (2.82×10^{-5})	NR (2.82×10^{-5})	

^aIf no cytotoxicity was reported, the highest concentration tested is reported in parenthesis

^bAfter the initial test was conducted, the laboratory changed the testing concentrations used, in order to more adequately cover the concentration-response curve

^cLaboratory voluntarily repeated testing.

Abbreviations: ECVAM = European Centre for the Validation of Alternative Methods; Hiyoshi = Hiyoshi Corporation; M = molar; NR = Not Reported; XDS = Xenobiotic Detection Systems, Inc.

Table 5-? Antagonist Viability Summary for Phase 2a, 2b, and 3 Comprehensive Experiments (Continued)

Chemical	Phase	Laboratory	Minimum Cytotoxic Concentration (M) ^{a,b,c}			
			Exp 1	Exp 2	Exp 3	Exp 4
Flavone	2b	XDS	1.12×10^{-4}	1.12×10^{-4}	2.25×10^{-4}	
		ECVAM	4.54×10^{-4}	4.54×10^{-4}	4.54×10^{-4}	
		Hiyoshi	4.54×10^{-4}	4.54×10^{-4}	4.54×10^{-4}	
Genistein	2b	XDS	NR (3.70×10^{-4})	3.70×10^{-4}	3.70×10^{-4}	
		ECVAM	3.70×10^{-4}	3.70×10^{-4}	3.70×10^{-4}	
		Hiyoshi	3.70×10^{-4}	3.70×10^{-4}	3.70×10^{-4}	
Resveratrol	2b	XDS	NR (4.38×10^{-4})	NR (4.38×10^{-4})	4.38×10^{-4}	
		ECVAM	NR (4.38×10^{-4})	4.38×10^{-4}	4.38×10^{-4}	
		Hiyoshi	NR (4.38×10^{-4})	NR (4.38×10^{-4})	NR (4.38×10^{-4})	
Actinomycin D	3	XDS	7.97×10^{-6}			
		ECVAM	9.96×10^{-8}			
		Hiyoshi	NR (7.97×10^{-5})			
Bisphenol A	3	XDS	8.76×10^{-5}			
		ECVAM	2.19×10^{-4}			
		Hiyoshi	2.19×10^{-4}			
Bisphenol B	3	XDS	5.16×10^{-5}			
		ECVAM	1.03×10^{-4}			
		Hiyoshi	5.16×10^{-5}			
Diethylstilbestrol	3	XDS	1.49×10^{-5}			
		ECVAM	9.32×10^{-5}			
		Hiyoshi	9.32×10^{-5}			
17- α Ethynodiol diacetate	3	XDS	3.37×10^{-4}			
		ECVAM	1.69×10^{-4}			
		Hiyoshi	1.69×10^{-4}			
4-Androstenedione	3	XDS	NR (3.49×10^{-4})			
		ECVAM	NR (3.49×10^{-4})			
		Hiyoshi	NR (3.49×10^{-4})			
Clomiphene citrate	3	XDS	3.34×10^{-5}			
		ECVAM	2.09×10^{-5}			
		Hiyoshi	6.69×10^{-5}			
Coumestrol	3	XDS	5.82×10^{-5}			
		ECVAM	NR (3.73×10^{-4})			
		Hiyoshi	NR (3.73×10^{-4})			

^aIf no cytotoxicity was reported, the highest concentration tested is reported in parenthesis

^bAfter the initial test was conducted, the laboratory changed the testing concentrations used, in order to more adequately cover the concentration-response curve

^cLaboratory voluntarily repeated testing.

Abbreviations: ECVAM = European Centre for the Validation of Alternative Methods; Hiyoshi = Hiyoshi Corporation; M = molar; NR = Not Reported; XDS = Xenobiotic Detection Systems, Inc.

Table 5-? Antagonist Viability Summary for Phase 2a, 2b, and 3 Comprehensive Experiments (Continued)

Chemical	Phase	Laboratory	Minimum Cytotoxic Concentration (M) ^{a,b,c}			
			Exp 1	Exp 2	Exp 3	Exp 4
4-Cumylphenol	3	XDS	1.18×10^{-4}			
		ECVAM	1.18×10^{-4}			
		Hiyoshi	1.88×10^{-4}			
Daidzein	3	XDS	7.87×10^{-4}			
		ECVAM	1.97×10^{-4}			
		Hiyoshi	9.83×10^{-4}			
Di - n -butyl phthalate	3	XDS	NR (3.59×10^{-3})	NR (3.59×10^{-3})		
		ECVAM	8.98×10^{-4}			
		Hiyoshi	1.80×10^{-3}			
<i>p,p'</i> -DDE	3	XDS	7.86×10^{-5}			
		ECVAM	1.57×10^{-4}			
		Hiyoshi	1.26×10^{-4}			
Diethylhexyl phthalate	3	XDS	NR (3.03×10^{-3})			
		ECVAM	NR (3.03×10^{-3})			
		Hiyoshi	NR (3.03×10^{-3})			
Dexamethasone	3	XDS	2.55×10^{-4}			
		ECVAM	NR (2.55×10^{-4})			
		Hiyoshi	1.27×10^{-3}			
5 <i>α</i> -Dihydrotestosterone	3	XDS	1.08×10^{-4}			
		ECVAM	NR (3.44×10^{-4})			
		Hiyoshi	NR (3.44×10^{-5})			
Dicofol	3	XDS	2.70×10^{-5}			
		ECVAM	6.75×10^{-5}			
		Hiyoshi	2.70×10^{-3}			
17- <i>α</i> Estradiol	3	XDS	9.18×10^{-5}			
		ECVAM	NR (3.67×10^{-4})			
		Hiyoshi	1.84×10^{-4}			
17- <i>β</i> Estradiol	3	XDS	NR (3.67×10^{-4})			
		ECVAM	3.67×10^{-3}			
		Hiyoshi	3.67×10^{-3}			
Ethyl paraben	3	XDS	3.01×10^{-3}			
		ECVAM	6.02×10^{-3}			
		Hiyoshi	6.02×10^{-3}			

^aIf no cytotoxicity was reported, the highest concentration tested is reported in parenthesis

^bAfter the initial test was conducted, the laboratory changed the testing concentrations used, in order to more adequately cover the concentration-response curve

^cLaboratory voluntarily repeated testing.

Abbreviations: ECVAM = European Centre for the Validation of Alternative Methods; Hiyoshi = Hiyoshi Corporation; M = molar; NR = Not Reported; XDS = Xenobiotic Detection Systems, Inc.

Table 5-? Antagonist Viability Summary for Phase 2a, 2b, and 3 Comprehensive Experiments (Continued)

Chemical	Phase	Laboratory	Minimum Cytotoxic Concentration (M) ^{a,b,c}			
			Exp 1	Exp 2	Exp 3	Exp 4
Estrone	3	XDS	4.62×10^{-5}			
		ECVAM	NR			
		Hiyoshi	(3.70×10^{-5})	3.70×10^{-4}		
Fluoranthene	3	XDS	1.24×10^{-4}			
		ECVAM	NR	(4.94×10^{-4})		
		Hiyoshi	NR	(4.94×10^{-3})		
<i>meso</i> -Hexestrol	3	XDS	1.85×10^{-4}			
		ECVAM	1.85×10^{-5}			
		Hiyoshi	1.48×10^{-4}			
Hydroxyflutamide	3	XDS	NR	(3.42×10^{-5})		
		ECVAM	NR	(3.42×10^{-4})		
		Hiyoshi	3.42×10^{-3}			
Kepone	3	XDS	6.38×10^{-5}			
		ECVAM	5.10×10^{-5}			
		Hiyoshi	1.63×10^{-5}	1.63×10^{-5}		
Kaempferol	3	XDS	3.49×10^{-4}			
		ECVAM	NR	(3.49×10^{-4})		
		Hiyoshi	1.75×10^{-3}			
<i>p,p'</i> -Methoxychlor	3	XDS	NR	(2.89×10^{-4})		
		ECVAM	7.23×10^{-4}			
		Hiyoshi	1.81×10^{-4}			
Morin	3	XDS	8.27×10^{-4}			
		ECVAM	NR	(3.31×10^{-4})		
		Hiyoshi	NR	(3.31×10^{-4})		
Methyl testosterone	3	XDS	2.07×10^{-4}			
		ECVAM	3.31×10^{-4}			
		Hiyoshi	NR	(3.31×10^{-4})		
Norethynodrel	3	XDS	4.19×10^{-6}			
		ECVAM	4.19×10^{-4}			
		Hiyoshi	2.09×10^{-4}			
4- <i>tert</i> -Octylphenol	3	XDS	6.06×10^{-5}			
		ECVAM	4.85×10^{-5}			
		Hiyoshi	3.88×10^{-5}			

^aIf no cytotoxicity was reported, the highest concentration tested is reported in parenthesis

^bAfter the initial test was conducted, the laboratory changed the testing concentrations used, in order to more adequately cover the concentration-response curve

^cLaboratory voluntarily repeated testing.

Abbreviations: ECVAM = European Centre for the Validation of Alternative Methods; Hiyoshi = Hiyoshi Corporation; M = molar; NR = Not Reported; XDS = Xenobiotic Detection Systems, Inc.

Table 5-? Antagonist Viability Summary for Phase 2a, 2b, and 3 Comprehensive Experiments (Continued)

Chemical	Phase	Laboratory	Minimum Cytotoxic Concentration (M) ^{a,b,c}			
			Exp 1	Exp 2	Exp 3	Exp 4
4-Hydroxy-tamoxifen	3	XDS	NR (2.58×10^{-4})			
		ECVAM	2.58×10^{-4}	2.58×10^{-4}		
		Hiyoshi	NR (2.58×10^{-6})			
Phenobarbital	3	XDS	NR (4.31×10^{-3})			
		ECVAM	NR (4.31×10^{-3})			
		Hiyoshi	Not Tested			
Phenolphthalin	3	XDS	NR (3.12×10^{-3})			
		ECVAM	NR (3.12×10^{-3})			
		Hiyoshi	3.12×10^{-3}			
Propylthiouracil	3	XDS	NR (5.87×10^{-3})			
		ECVAM	NR (5.87×10^{-3})			
		Hiyoshi	NR (5.87×10^{-3})			
Raloxifene HCl	3	XDS	1.96×10^{-8}			
		ECVAM	NR (1.96×10^{-8})			
		Hiyoshi	NR (1.96×10^{-8})			
Sodium azide	3	XDS	NR (1.54×10^{-3})			
		ECVAM	NR (1.54×10^{-3})			
		Hiyoshi	NR (1.54×10^{-3})			
2-sec-Butylphenol	3	XDS	NR (6.66×10^{-4})			
		ECVAM	2.66×10^{-4}			
		Hiyoshi	6.66×10^{-3}			
2,4,5-Trichloro-phenoxyacetic acid	3	XDS	NR (3.91×10^{-3})			
		ECVAM	NR (3.91×10^{-4})			
		Hiyoshi	NR (3.91×10^{-3})			

^aIf no cytotoxicity was reported, the highest concentration tested is reported in parenthesis

^bAfter the initial test was conducted, the laboratory changed the testing concentrations used, in order to more adequately cover the concentration-response curve

^cLaboratory voluntarily repeated testing.

Abbreviations: ECVAM = European Centre for the Validation of Alternative Methods; Hiyoshi = Hiyoshi Corporation; M = molar; NR = Not Reported; XDS = Xenobiotic Detection Systems, Inc.

Table 5-? Antagonist Viability Summary for Phase 2a, 2b, and 3 Comprehensive Experiments (Continued)

Chemical	Phase	Laboratory	Minimum Cytotoxic Concentration (M) ^{a,b,c}			
			Exp 1	Exp 2	Exp 3	Exp 4
Testosterone	3	XDS	4.33×10^{-4}			
		ECVAM	4.33×10^{-4}			
		Hiyoshi	NR (3.47×10^{-4})			
12 - O - Tetradecanoylphorbol-13-acetate	3	XDS	NR (1.62×10^{-5})	8.11×10^{-6}		
		ECVAM	3.24×10^{-5}			
		Hiyoshi	NR (1.62×10^{-3})			
Vinclozolin	3	XDS	NR (3.50×10^{-3})			
		ECVAM	NR (3.50×10^{-4})			
		Hiyoshi	6.99×10^{-4}			

^aIf no cytotoxicity was reported, the highest concentration tested is reported in parenthesis

^bAfter the initial test was conducted, the laboratory changed the testing concentrations used, in order to more adequately cover the concentration-response curve

^cLaboratory voluntarily repeated testing.

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Table 5-? Phase 4 Viability Summary Data

Chemical	AGONIST ^{a,b,c}		ANTAGONIST ^{a,b,c}	
	EXP #1	EXP #2	EXP #1	EXP #2
17 β -Trenbolone	3.70×10^{-4}	NR (3.70×10^{-5})	3.70×10^{-4}	NR (3.70×10^{-4})
19-Nortestosterone	NR (3.64×10^{-5})		NR (3.64×10^{-4})	
4-hydroxyandrostenedione	4.13×10^{-4}	NR (3.31×10^{-4})	NR (3.31×10^{-4})	
Ammonium perchlorate	NR (8.51×10^{-5})		NR (8.53×10^{-3})	
Apomorphine	3.74×10^{-5}		NR (3.74×10^{-4})	
Bicalutamide	NR (2.32×10^{-5})		NR (2.32×10^{-4})	
Chrysin	4.92×10^{-5}	NR (3.93×10^{-4})	NR (1.29×10^{-4})	
Cycloheximide	NR (3.55×10^{-6})		7.11×10^{-5}	
Cyproterone acetate	NR (2.40×10^{-3})	NR (2.40×10^{-5})	NR (2.40×10^{-4})	
Fenarimol	NR (3.02×10^{-4})	NR (3.02×10^{-5})	NR (3.02×10^{-3})	
Finasteride	NR (2.68×10^{-4})		NR (2.68×10^{-4})	
Fluoxymestrone	NR (2.97×10^{-4})		NR (2.97×10^{-3})	
Flutamide	NR (3.62×10^{-4})		NR (3.62×10^{-3})	
Haloperidol	NR (2.66×10^{-6})		NR (2.66×10^{-4})	
Ketoconazole	1.88×10^{-4}		9.41×10^{-6}	
L-Thyroxine	NR (1.29×10^{-4})	NR (1.29×10^{-5})	NR (1.29×10^{-4})	
Linuron	NR (8.03×10^{-5})	NR (4.01×10^{-5})	NR (4.01×10^{-3})	
Medroxyprogesterone acetate	NR (2.59×10^{-4})	2.59×10^{-4}	1.29×10^{-5}	
Mifepristone	NR (2.33×10^{-5})	2.33×10^{-5}	NR (2.33×10^{-3})	

^aIf no cytotoxicity was reported, the highest concentration tested is reported in parenthesis

^bAfter the initial test was conducted, the laboratory changed the testing concentrations used, in order to more adequately cover the concentration-response curve

^cLaboratory voluntarily repeated testing.

Abbreviations: ECVAM = European Centre for the Validation of Alternative Methods; Hiyoshi = Hiyoshi Corporation; M = molar; NR = Not Reported; XDS = Xenobiotic Detection Systems, Inc.

Table 5-? Phase 4 Viability Summary Data (Continued)

Chemical	AGONIST ^{a,b,c}		ANTAGONIST ^{a,b,c}	
	EXP #1	EXP #2	EXP #1	EXP #2
Nilutamide	NR (3.15×10^{-4})		3.15×10^{-3}	6.30×10^{-4}
Oxazepam	NR (3.49×10^{-6})		NR (3.49×10^{-4})	
Pimozide	NR (2.17×10^{-6})		2.17×10^{-5}	
Procymidone	NR (3.52×10^{-5})		3.52×10^{-4}	
Reserpine	NR (1.64×10^{-4})	NR (1.64×10^{-5})	NR (1.64×10^{-5})	
Spironolactone	NR (2.40×10^{-5})		NR (2.40×10^{-4})	

^aIf no cytotoxicity was reported, the highest concentration tested is reported in parenthesis^bAfter the initial test was conducted, the laboratory changed the testing concentrations used, in order to more adequately cover the concentration-response curve^cLaboratory voluntarily repeated testing.

Abbreviations: ECVAM = European Centre for the Validation of Alternative Methods; Hiyoshi = Hiyoshi Corporation; M = molar; NR = Not Reported; XDS = Xenobiotic Detection Systems, Inc.